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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,088	07/18/2003	Robert P. Bennett	IVGN 332	1853

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

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10/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,088	BENNETT ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to communication filed 7/13/2010.

Claims 45-56 are under current examination.

Any rejection(s) and/ or objection(s) not reiterated herein have been withdrawn.

Specification

The disclosure is objected to because of the following informalities: the instant specification lacks a description continuity data in its first line.

Appropriate correction is required.

Claim Rejections - 35 USC § 103-NECESSITATED BY AMENDMENT

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Yee (US Patent No. 5817491-see 892), von Melchner (*Blut*, 1988-previously cited), Ping (RNA, 1997-previously cited) and Hartley (*Genome Res*, 2000-previously cited).

The claims are drawn to (in part): a method of constructing a replication-incompetent-recombinant retrovirus, comprising:

(a) providing a first nucleic acid molecule lacking retroviral sequences which produce retroviral gene products and which comprises a 5'-long terminal repeat, a 3'-long terminal repeat, a packaging signal, and at least a first and a second recombination site that do not recombine with each other;

(b) contacting the first nucleic acid molecule with a second nucleic acid molecule comprising a sequence of interest flanked by at least a third and a fourth recombination site under conditions such that recombination occurs between the first and third recombination site and between the second and fourth recombination site; and

(c) introducing the nucleic acid molecule generated in step (b), with at least three additional nucleic acid molecules which encode retroviral proteins, into a cell that packages the nucleic acid molecule generated in step (b) such that the packaging signal of the first nucleic acid molecule is present *in trans* with respect to the at least three additional nucleic acid molecules which encode retroviral proteins; see claim 45.

Yee describes VSV G pseudotyped retroviral vector particle which includes retroviral gag and pol proteins and the VSV G envelope glycoprotein (see title and abstract; see instant claims 50 and 51, in part, claiming VSV G env). The author

describes making "safe" retroviruses via employing two components, a retroviral vector and a packaging cell. The retroviral vector contains LTRs, the foreign DNA (or gene of interest encoding a polypeptide) to be transferred and a packaging sequence. The packaging cell contains genes encoding the *gag*, *pol*, and *env* proteins with a downstream selectable marker but does not contain the packaging signal (see col. 2, lines 7+ and 27+ and FIG. 1A; instant claims 45, c, 46 and 54). Note that the described retroviral vector meets the structural limitations of the *resulting* nucleic acid following contacting the first and second nucleic acid of parts a and b of claim 45. Also, because Yee teaches the foreign gene is expressed by the host cell, an origin of replication must be inherently present (col. 2, lines 7+ and instant claim 52, in part). Yee describes using two separate molecules, carrying either the gag/pol or env packaging genes, for the advantage of decreasing the possibility of generating replication-competent virus via genetic interactions between the proviral vector DNA and the structural genes (col. 7, lines 48+ and col. 12, lines 18+; and instant claims 48 and 50, in part). Yee also notes that minimal sequences other than the protein coding sequences were used in order to decrease the possibility of homolgous recombination with the vector nucleic acid (see col. 12, lines 18+; and instant claim 47).

Note that von Melchner is only cited to show that a recombinant provirus comprises both a 3'- and 5'- LTRs; see Figure 1 and instant claim 45, a.

Yee and Von Melchner do not teach at least *three* separate nucleic acid molecules encoding retroviral proteins, including comprising a rev gene (instant claims

45, c and 50). It is noted here, however, that Yee describes *two* separate nucleic acid molecules, comprising gag/pol and env genes.

Yee and Von Melchner do not teach using recombination sites comprising either *att*R sites or *att*L sites on two separate molecules (claims 45, a and b, and 56).

Yee and von Melchner do not teach digesting the first nucleic acid with a restriction enzyme that cleaves the first nucleic acid at a restriction site between recombination sites (instant claim 55).

Ping describes that the gene expression of HIV-1 depends on the interactions of viral regulatory proteins, including Rev. Specifically, Rev acts post-transcriptionally to increase the cytoplasmic accumulation of the viral gag-pol and env mRNA (see Introduction).

Hartley describes a method of DNA cloning using site-specific recombination between two molecules (see whole document). See Figure 1B which depicts two separate DNA molecules in which one molecule contains 2 *att*L sites and a gene of interest and the other contains 2 *att*R sites (claims 45, a and b, and 56). The legend to Figure 3 describes the unique NcoI site and the T7 promoter of the destination vector (instant claim 55). Also, there must also inherently be an origin of replication given the DNA is copied following transformation of bacterial cells (see p. 1791, col. 2 and minipreps, p. 1795). The author describes the *in vitro* site-specific recombination method as a method allowing numerous DNA segments to be transferred in parallel into many vector backgrounds (see Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to further incorporate a third nucleic acid in the method described by Yee and von Melchner. One would have been motivated to do so for the advantage of increasing cytoplasmic accumulation of the viral gag/pol and env mRNA (as taught by Ping). There would have been reasonable expectation of success given that rev has been characterized by the prior art and the underlying techniques are commonly known and widely used (e.g. gene expression of known genes, etc.).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the recombination method described by Hartley in the method of Yee and von Melchner. One would have been motivated to do so as a means of inserting the gene of interest into the retroviral vector (components a and b of claim 45). There would have been reasonable expectation of success given this technique is widely known and commonly used as shown by the applied prior art.

The invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claim is allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ZACHARIAH LUCAS can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Supervisory Patent Examiner, Art Unit 1648